

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

Please add new claims 167-172.

1-122 (Cancelled)

123. (Currently amended) A method for promoting one or more of growth, differentiation, and survival of neuronal cells in culture, comprising contacting said cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence at least 80% identical to at least one sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 50 contiguous amino acid residues thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells in culture.

124. (Currently amended) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells in culture with an effective amount of a *hedgehog* polypeptide comprising an amino acid sequence at least 80% identical to at least one sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 50 contiguous amino acid residues thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to increase the survival of the neuronal cells in culture.

125. (Currently amended) A method for promoting growth, differentiation, or survival of mammalian ~~neuronal~~ neural stem cells in culture, comprising treating the cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence at least 80% identical to at least one sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 50 contiguous amino acid residues thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein the amount

of the *hedgehog* polypeptide is effective to increase the rate of growth of the ~~neuronal~~ neural stem cells in culture.

126. **(Previously added)** The method of any one of claims 123, 124, or 125, wherein said *hedgehog* polypeptide is administered in combination with one or more other neurotrophic factors.

127. **(Previously added)** The method of claim 126, wherein said other neurotrophic factor is selected from CNTF, BDNF, and NGF.

128. **(Previously added)** The method of claim 123, wherein said neuronal cells are neural progenitor cells.

129. **(Previously added)** The method of claim 123, wherein said neuronal cells differentiate into cells having a selected neural phenotype.

130. **(Previously added)** The method of claim 129, wherein said neuronal cells differentiate into cells of the central nervous system or the peripheral nervous system.

131. **(Cancelled)**

132. **(Cancelled)**

133. **(Currently amended)** The method of any one of claims ~~claim~~ 123, 124, or 125, wherein said *hedgehog* polypeptide comprises an amino acid sequence identical to ~~with~~ an amino acid sequence designated in one of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 150 ~~50~~ contiguous amino acid residues thereof.

134. **(Previously amended)** The method of any one of claims 123, 124, or 125, wherein said *hedgehog* polypeptide has an amino acid sequence which is encoded by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.

135. **(Currently amended)** The method of claim 123, wherein said *hedgehog* polypeptide comprises an amino acid sequence ~~is encoded by a nucleic acid which~~ is at least 98% identical ~~with to~~ at least one of a ~~nucleic~~ amino acid sequence designated in SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of at least ~~150 contiguous nucleotides~~ thereof.

136. **(Currently amended)** The method of claim 123, wherein said *hedgehog* polypeptide comprises an amino acid sequence ~~is encoded by a nucleic acid which~~ is at least 90% identical ~~with to~~ at least one of a ~~nucleic~~ amino acid sequence designated in SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of at least ~~150 contiguous nucleotides~~ thereof.

137. **(Currently amended)** The method of claim 123, wherein said *hedgehog* polypeptide comprises an amino acid sequence ~~is encoded by a nucleic acid which~~ is at least 95% identical ~~with to~~ at least one of a ~~nucleic~~ amino acid sequence designated in SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of at least ~~150 contiguous nucleotides~~ thereof.

138. **(Currently amended)** The method of ~~any one of claims~~ claim 123, 124, or 125, wherein said polypeptide includes a *hedgehog* amino acid sequence ~~at least 90 percent identical to~~ with a sequence selected from residues 104-189 of SEQ ID NO: 8, residues 102-187 of SEQ ID NO: 11, or residues 101-186 of SEQ ID NO: 12.

139. **(Currently amended)** The method of ~~any one of claims~~ claim 123, 124, or 125, wherein said polypeptide includes a *hedgehog* amino acid sequence ~~at least 90 percent identical to~~ with a sequence selected from residues 27-189 of SEQ ID NO: 8, residues 25-187 of SEQ ID NO: 11, or residues 24-186 of SEQ ID NO: 12.

140. **(Currently amended)** The method of ~~any one of claims~~ claim 123, 124, or 125, wherein said polypeptide includes a *hedgehog* amino acid sequence ~~at least 90 percent identical to~~ with an amino acid sequence selected from residues 27-425 of SEQ ID NO: 8, residues 25-437 of SEQ ID NO: 11, residues 24-418 of SEQ ID NO: 12, or residues 24-475 of SEQ ID NO: 13.

141. **(Previously added)** The method of claim 123, wherein said polypeptide includes an amino acid sequence encoded by a naturally occurring vertebrate *hedgehog* gene.

142. **(Previously added)** The method of claim 141, wherein said *hedgehog* gene is a mammalian *hedgehog* gene.

143. **(Previously added)** The method of claim 142, wherein said *hedgehog* gene is a human *hedgehog* gene.

144. **(Currently amended)** The method of any one of claims claim 123, 124, or 125, wherein said polypeptide includes an amino acid sequence which is encoded by at least a portion of a *hedgehog* gene of vertebrate origin selected from nucleotides 64-567 of SEQ ID NO: 1, nucleotides 73-561 of SEQ ID NO: 4, and nucleotides 70-558 of SEQ ID NO: 5.

145. **(Cancelled)**

146. **(Previously added)** The method of claim 123, wherein said polypeptide includes at least 150 contiguous amino acid residues of the N-terminal half of a *hedgehog* protein.

147. **(Previously added)** The method of claim 123, wherein said polypeptide binds to a naturally occurring *patched* receptor.

148. **(Previously added)** The method of claim 147, wherein said *patched* receptor is a patched receptor of a vertebrate organism.

149. **(Previously added)** The method of claim 123, wherein said neuronal cells are selected from motor neurons, cholinergic neurons, dopaminergic neurons, serotonergic neurons and peptidergic neurons.

150. **(Cancelled)**

151. **(Previously added)** The method of claim 123, wherein said polypeptide includes at least 50 contiguous amino acid residues of the N-terminal half of a *hedgehog* protein.

152. **(Previously added)** The method of claim 123, wherein said polypeptide includes at least 100 contiguous amino acid residues of the N-terminal half of a *hedgehog* protein.

153. **(Currently amended)** A method for promoting one or more of growth, differentiation, and survival of neuronal cells in culture, comprising contacting said cells with an amount of a *hedgehog* polypeptide encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in ~~one~~ any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, ~~or an N-terminal fragment thereof of at least 150 contiguous nucleotides~~, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of a *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells in culture.

154. **(Currently amended)** A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells in culture with an amount of a *hedgehog* polypeptide effective to promote the survival of neuronal cells in culture, wherein said *hedgehog* polypeptide is encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in ~~one~~ any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, ~~or an N-terminal fragment thereof of at least 150 contiguous nucleotides~~, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor.

155. **(Currently amended)** A method for promoting growth of mammalian ~~neuronal~~ neural stem cells in culture, comprising treating the cells with an amount of a *hedgehog* polypeptide ~~encoded~~ encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in ~~one~~ any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, ~~or an N-terminal fragment thereof of at least 150 contiguous nucleotides~~, wherein said *hedgehog* polypeptide binds to a naturally

occurring *patched* receptor, and wherein said amount of a *hedgehog* polypeptide is effective to increase the rate of growth of the ~~neuronal~~ neural stem cells in culture.

156. **(Currently amended)** The method of claim 125, wherein said polypeptide ~~sequence~~ comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence ~~which is~~ at least 90% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 ~~contiguous nucleotides~~ thereof.

157. **(Currently amended)** The method of claim 125, wherein said polypeptide ~~sequence~~ comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence ~~which is~~ at least 95% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 ~~contiguous nucleotides~~ thereof.

158. **(Currently amended)** The method of claim 125, wherein said polypeptide ~~sequence~~ comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence ~~which is~~ at least 98% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 ~~contiguous nucleotides~~ thereof.

159. **(Currently amended)** The method of claim 124, wherein said polypeptide ~~sequence~~ comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence ~~which is~~ at least 90% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 ~~contiguous nucleotides~~ thereof.

160. **(Currently amended)** The method of claim 124, wherein said polypeptide ~~sequence~~ comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence ~~which is~~ at least 95% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 4, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 ~~contiguous nucleotides~~ thereof.

161. **(Currently amended)** The method of claim 124, wherein said polypeptide ~~sequence~~ comprises a ~~polypeptide encoded by a nucleic acid sequence~~ an amino acid sequence which is at least 98% identical to a ~~nucleic acid sequence~~ an amino acid sequence designated in one of SEQ ID NO: ~~8~~ 4, SEQ ID NO: ~~11~~ 4, SEQ ID NO: ~~12~~ 5, SEQ ID NO: ~~13~~ 6, or an N-terminal auto-proteolytic fragment of ~~150~~ contiguous nucleotides thereof.

162. **(Previously added)** The method of claim 123, wherein the N-terminal fragment is approximately 19 kD.

163. **(Previously added)** The method of claim 124, wherein the N-terminal fragment is approximately 19 kD.

164. **(Previously added)** The method of claim 125, wherein the N-terminal fragment is approximately 19 kD.

165. **(Currently amended)** The method of claim ~~128~~ 123, wherein said neural progenitor ~~neuronal~~ cells differentiate into glial cells.

166. **(Currently amended)** The method of claim ~~125~~ 129, wherein said ~~neuronal~~ neural stem cells differentiate into glial cells.

167. **(New)** The method of claim 123, wherein said polypeptide comprises an amino acid sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof.

168. **(New)** The method of claim 124, wherein said polypeptide comprises an amino acid sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof.

169. **(New)** The method of claim 125, wherein said polypeptide comprises an amino acid sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof.

170. (New) A method for promoting one or more of growth, differentiation, and survival of neuronal cells in culture, comprising contacting said cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence identical to an amino acid sequence designated in any of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells in culture.

171. (New) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells in culture with an effective amount of a *hedgehog* polypeptide comprising an amino acid sequence identical to an amino acid sequence designated in any of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to increase the survival of the neuronal cells in culture.

172. (New) A method for promoting growth, differentiation, or survival of mammalian neural stem cells in culture, comprising treating the cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence identical to an amino acid sequence designated in any of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein the amount of the *hedgehog* polypeptide is effective to increase the rate of growth of the neural stem cells in culture.